Secondary Degeneration of the Substantia Nigra and Corticospinal Tract after Hemorrhagic Middle Cerebral Artery Infarction: Diffusion-weighted MR Findings

Toshibumi Kinoshita*, Toshio Moritani, David A. Shrier, Henry Z. Wang, Akio Hiwatashi, Yuji Numaguchi, and Per-Lennart A. Westesson

Department of Radiology, Division of Neuroradiology, University of Rochester Medical Center
601 Elmwood Ave. Box 648, Rochester, NY 14642, USA
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Middle cerebral artery (MCA) infarction involving the striatum can cause secondary degeneration of the substantia nigra and corticospinal tract. We present a patient with subacute hemorrhagic MCA infarction in whom diffusion-weighted MR images showed high signal intensity in the ipsilateral substantia nigra and corticospinal tract. A corresponding apparent diffusion coefficient map revealed a uniformly decreased signal in the same area. This represents secondary degeneration and should not be mistaken for other pathological conditions, such as a new infarction.

Keywords: cerebral infarction, degeneration, substantia nigra, MRI, diffusion-weighted

Introduction

Cerebral infarction in the territory of the middle cerebral artery (MCA) often induces trans-synaptic degeneration in the ipsilateral substantia nigra and wallerian degeneration of the corticospinal tract.¹⁻³ Previous studies have shown that diffusion-weighted imaging (DWI) can demonstrate the wallerian degeneration in the subacute period.⁴⁻⁵ However, DWI signal alterations in the ipsilateral substantia nigra have been demonstrated only in rats.⁶⁻⁷ We report DWI abnormalities in the ipsilateral substantia nigra in a patient with a subacute MCA infarct.

Case Report

A 76-year-old woman with a history of hypertension and hypercholesterolemia was admitted to the hospital 12 hours after onset of lethargy and profound left-sided weakness. At the time of admission, she had decreased sensation to pain and temperature on the left side. CT showed loss of gray-white matter differentiation, early gyral swelling, and parenchymal hypodensity in the right MCA territory, consistent with acute right MCA infarction. No intravenous anticoagulation was undertaken.

Over the next few days, the patient became more alert; however, her left hemiparesis continued. On the eighth day after admission, she underwent MR imaging. T2-weighted images showed high signal intensity and mild swelling in the right MCA territory (Fig. 1a, b). T2-weighted images showed markedly increased signal intensity in the right substantia nigra and slightly increased signal intensity in the right cerebral peduncle. The right substantia nigra demonstrated a focus of increased signal on T2-weighted images (Fig. 1a). DWI was performed using two levels of diffusion sensitization (b = 0 and 1000 s/mm²) acquired in three orthogonal orientations to calculate the apparent diffusion coefficient (ADC). DWI revealed high signal intensity in the pars reticulata of the right substantia nigra, the right cerebral peduncle, the posterior limb of the right internal capsule, and the right MCA territory (Fig. 1c, d). The pars compacta of the substantia nigra was spared on DWI. The posterior part of the right putamen on both b = 0 and b = 1000 images exhibited a low signal, indicating deposition of hemoglobin degradation products (Fig. 1d). ADC maps showed markedly decreased signal in the pars reticulata of the right substantia nigra, the right cerebral peduncle, and the posterior limb of the
Fig. 1. MR images obtained eight days after onset

a, b: T2-weighted images, c, d: Echo-planar diffusion-weighted images, e, f: ADC maps

T2-weighted images demonstrate the hyperintense area in the right substantia nigra (arrow), in addition to MCA infarction with involvement of the striatum. Diffusion-weighted images reveal a high signal area in the pars reticulata of the right substantia nigra and cerebral peduncle (arrow). The pars compacta of the substantia nigra is spared (arrowheads). A high signal area is noted in the posterior limb of the right internal capsule. The MCA infarction showing high signal intensity includes a low intensity area in the posterior part of the right putamen. Corresponding ADC maps show a marked decrease in ADC in the right substantia nigra and cerebral peduncle. ADC in the posterior limb of the right internal capsule is moderately decreased; ADC in the infarcted area is mildly decreased.
right internal capsule (Fig. 1e, f). The ADC values were lower on the right affected side versus the left unaffected side; right substantia nigra (0.458 × 10⁻³ mm²/s) versus left substantia nigra (0.822 × 10⁻³ mm²/s), right cerebral peduncle (0.498 × 10⁻³ mm²/s) versus left cerebral peduncle (0.761 × 10⁻³ mm²/s), and right internal capsule (0.574 × 10⁻³ mm²/s) versus left internal capsule (0.726 × 10⁻³ mm²/s). On ADC maps, the signal intensity of the right MCA infarction was heterogeneous and mildly decreased, while the ADC of the posterior part of the right putamen, which showed low intensity on b₀ images, was not significantly elevated or decreased. Contrast-enhanced T₁-weighted images showed no definite enhancement in the midbrain, while marked contrast enhancement was seen in the right MCA infarction. The results of this MR examination are compatible with subacute hemorrhagic infarction of the MCA territory. The changes in the substantia nigra and corticospinal tract are far more likely to represent secondary degeneration, as they do not correspond to the vascular distribution of the primary infarction within the cerebral hemisphere. Lack of contrast enhancement is consistent with secondary degeneration of the substantia nigra and corticospinal tract after MCA infarction.

The patient had persistent hemiparesis on the left and remained aphasic with severe dysarthria. She was referred to another facility for rehabilitation on hospital day 12.

Discussion

Focal cerebral infarction often results in delayed neuronal degeneration in areas connecting to the infarcted region. The reason for this has been unclear, but long-term intraventricular infusion of the γ-aminobutyric acid (GABA) agonist muscimol has been shown to prevent neuronal death. It is now thought that neuronal death in the ipsilateral substantia nigra after striatal injury is due to excessive excitation induced by a loss of the inhibitory transmitter GABA. Therefore, secondary degeneration in the substantia nigra may be caused by trans-neuronal mechanism.

Secondary degeneration in the substantia nigra appears as high signal lesions on T₂-weighted MR images 7–12 days after MCA stroke involving the striatum. Lack of contrast enhancement is characteristic of secondary degeneration because of the integrity of the blood-brain barrier and the absence of reactive neovascularization. Since the substantia nigra is spared in patients with MCA infarction without a striatal infarct, striatal injury predisposes the patient to secondary degeneration of the substantia nigra.

A decrease in ADC of the substantia nigra after striatal infarction has not been documented in human subjects to our knowledge. Our case shows that DWI may reveal high signal areas with decreased ADC in the ipsilateral substantia nigra secondary to MCA infarction in the subacute period. In rats with MCA occlusion, a transient decrease in ADC was noted in the ipsilateral substantia nigra during the subacute phase of cerebral infarction. Zhao et al reported the rat MCA occlusion model to correlate MR characteristics of trans-synaptic degeneration in the substantia nigra with associated histologic changes. A histologic examination in the subacute period revealed dark-staining neurons, markedly swollen perivascular astrocytic end-feet, and numerous swollen neurons with cyttoplasmic microvacuoles, while reactive astrocytes and dark neurons most frequently appeared in the chronic period. Since the severity of cellular swelling paralleled the change in the ADC, decreased ADC might be due to cellular swelling with decreased motion of the extracellular water. This experimental study suggests that restricted water diffusion is due to swelling of astrocytes and neurons accompanied by trans-synaptic degeneration. The swelling of astrocytic end-feet was observed, especially in the pars reticulata. The pars reticulata of the substantia nigra might be affected with sparing of the pars compacta of the substantia nigra in patients with striatal infarction, as seen in our case.

Wallerian degeneration is easily recognized pathologically in the corticospinal tract after MCA infarction. This descending motor tract arises in the precentral gyrus and surrounding cerebral cortex and extends through the ipsilateral corona radiata, the posterior limb of the internal capsule, and the specific locations in the cerebral peduncle, pons, and medulla. During the early period of wallerian degeneration, the distal part of the axon fragments and the surrounding myelin sheaths break down into a series of myelin ovoids. Although T₂ signal changes due to wallerian degeneration are usually invisible during the first month, early T₂ prolongation due to wallerian degeneration is occasionally demonstrated. DWI can depict this wallerian degeneration as high signal lesions along the corticospinal tract within two weeks following onset. Although ADC reportedly increases in wallerian degeneration, the findings of the present study demonstrated restriction of water diffusion within areas of wallerian degeneration in the early phase. An accumulation of myelin debris from
the breakdown of axons may hinder water molecule motion. Alternatively, increased astrocytes and microglia would be expected to restrict the mobility of water molecules to a lesser extent.\textsuperscript{10} In this case, almost the entire cerebral peduncle showed high signal intensity with decreased ADC on diffusion-weighted images. Therefore, frontopontine cortico-bulbar and temporoparietooccipitopontine tracts as well as the corticospinal tract might also be effected in the process of wallerian degeneration following widespread cortical infarction, as previously described.\textsuperscript{4,13}

The decreases in ADC in the substantia nigra and corticospinal tract were greater than the decreases in ADC in the infarcted areas during the subacute period of cerebral infarction. The milder decrease in ADC in the infarcted areas likely reflects the development of vasogenic edema and cell membrane disruption, leading to increased extracellular water and a relative increase in ADC.\textsuperscript{14} Hemorrhagic conversion may occur during the subacute period. Hemorrhagic foci may show pronounced low intensity on echo-planar spin-echo T2-weighted images because of T2 shortening and the paramagnetic susceptibility effect.\textsuperscript{15}

MR diagnosis of secondary degeneration following an MCA stroke rests on the characteristic locations. DWI with ADC maps clearly demonstrate the early changes of secondary degeneration of the substantia nigra and corticospinal tract ipsilateral to the MCA infarction. The clinical significance of our observation is that DWI signal abnormalities should not be interpreted as a new infarction but rather as secondary neuronal degeneration due to the original infarct.

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References